Citation:

Berglund L, Lefevre M, Ginsberg HN, Kris-Etherton PM, Elmer PJ, Stewart PW, Ershow A, Pearson TA, Dennis BH, Roheim PS, Ramakrishnan R, Reed R, Stewart K, Phillips KM; DELTA Investigators. Comparison of monounsaturated fat with carbohydrates as a replacement for saturated fat in subjects with a high metabolic risk profile: studies in the fasting and postprandial states. *Am J Clin Nutr.* 2007 Dec; 86 (6): 1,611-1,620

PubMed ID: 18065577

Study Design:

Randomized Crossover Trial

Class:

A - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

- To determine whether the replacement of dietary saturated fat with monounsaturated fat, as opposed to carbohydrate, would result in a better overall risk factor profile in non-diabetic individuals with one or more of the following: Low HDL-cholesterol, high triacylglycerol, or high insulin concentrations
- To evaluate two separate postprandial conditions
- To explore whether the diet response would differ depending on baseline lipid concentrations or the presence of the metabolic syndrome and insulin resistance.

Inclusion Criteria:

- Aged 21-65 years
- Likely at risk of the potential negative effects of low-fat diets; meaning the average of two screening measurements met the following: HDL ≤30th percentile, triacylglycerol ≥70th percentile and insulin ≥70th percentile
- In good health, free of chronic disease and taking no medications known to affect lipids or thrombotic factors.

Exclusion Criteria:

- Average screening total cholesterol <25th percentile or >90th percentile
- LDL >4.91mmol/L
- Fasting triacylglycerol <30th percentile or >5.65mmol/L
- HDL >70th percentile.

Description of Study Protocol:

Recruitment

Recruitment methods not described

Design

Randomized crossover trial. Three diets fed in a double-blind, three-way crossover with each diet lasting seven weeks with a rest period of four to six weeks between each diet. All food was provided except for a self-selected meal on Saturday evenings. The meal was to follow the NCEP Adult Treatment Panel Step I guidelines.

Blinding used

Double-blind

Intervention

- Average American diet (AAD) to reflect the typical pattern of US population
- Carbohydrate-replacement diet (CHO diet) to meet the nutrient specifications of the NCEP Step I diet. It contained more fiber than the AAD.
- Monounsaturated fat-replacement diet (MUFA diet) to match the saturated (SFA) and polyunsaturated fat content of the CHO diet but also the total fat of the AAD
- Seven percent of energy from SFAs was replaced with either CHO (primarily complex) on the CHO diet or with MUFAs on the MUFA diet
- All three diets provided 300mg cholesterol per day.

Statistical Analysis

The linear statistical model, the set of primary hypotheses, the strategy for controlling type I error and the estimation procedures were all specified a priori. $P<0.01$ as chosen as statistically significant.

Data Collection Summary:

Timing of Measurements

Blood samples at weeks five, six and seven of each of the three diets. Weights twice weekly. Two day-long studies during week seven of each diet to study the effect of eating natural food and a high-fat load.

Dependent Variables

- Total cholesterol, LDL, HDL, triacylglycerol, glucose, uric acid (enzymatic assay)
- Apolipoprotein (apo) A-1 and apo B (rate immunonephelometry)
- Lipoprotein(a) [Lp(a)] (enzyme-linked immunosorbent assay)
- Insulin (radioimmunoassay)
- Insulin resistance (homeostasis model assessment of insulin resistance (HOMA-IR) index).

Independent Variables

- Average American diet (16% protein, 47% CHO, 37% fat [16% SFA, 14% MUFA, 7%

PUFA]),7.5g fiber, 300mg cholesterol
- CHO diet (16% protein, 54% CHO, 30% fat [8%SFA, 15% MUFA, 7% PUFA]),15g fiber, 300mg cholesterol
- MUFA diets (16% protein, 47% CHO, 37% fat [8%SFA, 22% MUFA, 7% PUFA]),7.5g fiber, 300mg cholesterol
- High fat load meal: 105g fat (52g SFA), 48g CHO, 32g protein, 300mg cholesterol and 1,237 calories per 2 m^2 body surface area.

Control Variables

Description of Actual Data Sample:

- ***Initial N:*** 110
- ***Attrition (final N):*** 85 for all three diets (33 females)
- ***Age:*** 35.5±9.4 (range 21-61 years)
- ***Ethnicity:*** 10 African Americans
- ***Other relevant demographics:*** Not applicable
- ***Anthropometrics:*** Not applicable
- ***Location:*** New York, Louisiana, Pennsylvania, Minnesota.

Summary of Results:

Key Findings

- Relative to the average American diet, LDL cholesterol was lower with both the CHO (-7.0%) and MUFA (-6.3%) diets, whereas the difference in HDL cholesterol was smaller during the MUFA diet (-4.3%) than during the CHO diet (-7.2%)
- Plasma triacylglycerols tended to be lower with the MUFA diet, but were significantly higher with the CHO diet
- Postprandial triacylglycerol concentrations did not differ significantly between the diets
- Lipoprotein (a) concentrations increased with both the CHO (20%) and MUFA (11%) diets relative to the average American diet.

Table: Effect of Diet on Primary End-points

Variables	AAD	MUFA diet	CHO diet
Total cholesterol (mmol/L)	5.17±0.08	4.86±0.08[2]	4.89±0.08[2]
LDL cholesterol (mmol/L)	3.31±0.08	3.10±0.08[2]	3.08±0.08[2]
HDL cholesterol (mmol/L)	1.08±0.03	1.03±0.03[2]	1.00±0.02[2,3]
Triacylglycerols (mmol/L)	1.48±0.038	1.42±0.07	1.59±0.08[2,3]
Apolipoprotein A-1 (mg/dL)	128±2	125±2[2]	122±2[2]
Apolipoprotein B-1 (mg/dL)	110±3	106±2[2]	107±2[2]
Lipoprotein (a) (mg/dL)	9.9±1.4	11.0±1.5[2]	11.9±1.6[2]
Glucose (mmol/L)	5.1±0.1	5.1±0.1	5.1±0.1

Insulin (µU/mL)	12.2±0.6	12.3±0.6	12.1±0.7

All values are mean ± SEM, except for triacylglycerols and Lp(a), which are medians ± SEM.

[2]Significantly different from AAD on the basis of adjusted values from the a priori linear regression model, P<0.01.

[3]Significantly different from MUFA diet on the basis of adjusted values from the a priori linear regression model, P<0.01.

Other Findings

- Triacylglycerol concentrations with the AAD diet were significantly higher in subjects with metabolic syndrome (N=20; 12 men and eight women) or with insulin resistance (N=28; 18 men and 10 women) than in subjects who did not fulfill these criteria
- Glucose concentrations were lower in the post-lunch phase of the day-long study for the CHO diet. Insulin concentrations were highest with the AAD diet during the day-long study.

Author Conclusion:

In individuals considered at increased risk of CAD, the replacement of dietary SFA with MUFA rather than CHO is preferred because of associated smaller reduction in HDL cholesterol and a trend toward a reduction in fasting triacylglycerol concentrations. Dietary recommendations based on underlying risk factors may be a more effective approach for CAD prevention.

Reviewer Comments:

All foods provided. Authors note the following limitations:

Subjects' weights were maintained, so the issue of dietary effects on lipid concentrations under free-living conditions is unknown.

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes

4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	Yes
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	Yes
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes

7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	N/A
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes